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Occurrence, predictive factors and associated morbidity of bronchopulmonary dysplasia in a preterm birth cohort

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1 Introduction

Respiratory diestress is still an important cause of morbidity and mortality among preterm infants in spite of recent advances in its treatment and prevention [1, 2]. Although most infants with respiratory distress syndrome (RDS) have an uneventful recovery, a considerable proportion – from 6% to 69% of those requiring respirator treatment – suffer from bronchopulmonary dysplasia (BPD), which sometimes requires hospitalization lasting several months [3–9]. These percentages vary with the definitions used and with the composition of groups examined, which are usually selected materials from single institutions.

In this report we describe the occurrence of BPD in a preterm birth cohort born in the province of Kuopio, Finland, during 1978–82. The study area is characterized by a low rate of prematurity, government-subsidized antenatal care and regionalization of obstetric and neonatal services [10]. The role of perinatal factors and the predictive value of certain early radiologic criteria were also investigated in relation to the subsequent development of BPD. Finally, the impact of BPD on postneonatal morbidity was examined both in relation to chronic prematurity-associated conditions and to more acute diseases requiring intermittent hospital care.

2 Patients and methods

2.1 Patients

Kuopio University Central Hospital serves a population of 253,900 inhabitants (31. 12. 1982). During the study period (1978–82) a total of 17,019 neonates were born in this area. Seven hundred and twelve children (4.2%) were born prematurely at < 37 weeks of gestation. Twenty-three children with malformations were excluded from the analysis. For preterm births, the corrected perinatal mortality rate (PMR) without malformations was 123/1000 (stillbirths 91/1000, first week mortality 32/1000). Corrected neonatal and postneonatal MRs were 41/1000 and 7/1000, respectively.

In this cohort, BPD was found exclusively among preterms born at or before 32 weeks of gestation [11]. Of these, 77% (91 of 118) survived the neonatal period and 75% (88 of 118) were alive at the age of two years. These children were followed-up in a neonatal outpatient clinic up to at least two years of age. Developmental assessments were made at 3, 6, 12 and 24 months of corrected age.

Curriculum vitae

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2.2 Definitions

Entities of neonatal morbidity and care, examined in relation to BPD, consisted of intrauterine growth status, RDS, pulmonary air leaks, respirator treatment and its duration, oxygen requirement, problems of metabolic adaptation (hypoglycemia, hypocalcemia, hyperbilirubinemia) and surgical diseases, particularly necrotizing enterocolitis. The definitions where pertinent are presented in table I. In order to verify the diagnosis of both RDS and BPD, all chest X-rays of cohort members were reviewed by the radiologist (O. K.).

Postneonatal morbidity was defined as consisting of all hospital readmissions after discharge from the neonatal intensive care unit. These data were collected from the hospital records of the study children as soon as they reached the age of two years. The number, duration and causes of readmissions were documented. The readmission diagnoses were grouped as follows: chronic prematurity-associated conditions and more acute disorders, requiring intermittent care and with relatively favorable outcome.

Chronic prematurity-associated morbidity consisted, in addition to BPD, mainly of various forms of cerebral palsy (CP) and retrolental fibroplasia (RLF). BPD was diagnosed if oxygen treatment for the maintenance of normal transcutaneous oxygen partial pressure was still necessary at or after 28 days of life, and if chronic changes were present in the lungs [12]. All preterms with respiratory difficulties after extubation underwent bronchoscopy for detection of subglottic stenosis. CP was defined according to D'AVIGNON et al. [13]. RLF was diagnosed and classified according to fundoscopic findings [14]. Other, non-chronic postneonatal morbidity consisted of various forms of respiratory tract infections, other infections, surgery and behavioral problems.

Table I. Neo- and postneonatal morbidity of BPD and non-BPD children.

	BPD n = 16	non-BPD n = 75[1]	p
Neonatal	%	%	
IUGR (birth weight more than 2 SD below the expected mean for gestational age)	12	14	ns
Low (< 7) 1 minute Apgar score	75	40	< 0.05
Low (< 7) 5 minute Apgar score	69	7	= 0.01
RDS (prematurity, respiratory distress from birth, typical radiologic signs, blood culture negative)	100	27	< 0.001
Pulmonary air leaks	18	5	ns
Pneumonias or atelectases	50	7	< 0.001
Convulsions or apneic episodes	44	12	< 0.01
Hypocalcemia (S-Ca < 1.74 mmol/l)	56	29	= 0.05
Hyperbilirubinemia (phototherapy or exchange transfusion)	75	67	ns
Hypoglycemia (B-gluc < 1.7 mmol/l)	2	1	ns
Necrotizing enterocolitis	0	4	ns
Postneonatal	%	%	
Chronic conditions			
Severe[2] or	25	9	ns
moderate[2] neurologic signs	12	6	ns
Retrolental fibroplasia	12	0	< 0.01
Subglottic stenosis	19	1	< 0.01
Respiratory infections	63	20	= 0.05
Surgical infections	18	13	ns
Behavioral (feeding, sleeping) problems	6	2	ns

[1] The non-BPD subgroup born at ≤ 30 weeks (26 cases) has been combined with that born between 31–32 weeks (49 cases) because no significant difference in any of the morbidity items was observed between them.
[2] Severe= CP syndromes or grave mental retardation; Moderate = convulsions, hydrocephalus or delayed psychomotor development.

2.3 Study design

Our primary aim was to assess the incidence of BPD, defined as the number of new cases of BPD per 1000 live preterm births per time period [15], in a regionally representative preterm birth cohort.

The analysis of neonatal morbidity was begun by identifying neonatal variables which were present significantly more often among BPD (16 children) than non-BPD preterms (75 children). The non-BPD children were divided into two groups: very preterm infants born at or before 30 weeks of gestation (26 children) and more mature children born at 31–32 weeks of gestation (49 children). This design made it possible to compare the morbidity of BPD children with that associated with different degrees of gestational maturity. Only if no differences in morbidity could be shown between the non-BPD groups were they combined. Subsequently, the value of pertinent neonatal variables as predictors of BPD were estimated. Similarly, patterns of postneonatal morbidity (up to the age of two years) among BPD and non-BPD groups were compared. Chronic, prematurity-associated conditions and short-term intermittent care for more benign disorders (e.g. respiratory infections, surgical diseases and certain behavioral problems) were analyzed separately.

Increasing severity of RDS is also said to increasingly predispose preterm infants to BPD [3]. To test this hypothesis all chest X-rays (without other clinical information) taken from RDS patients (54 children) during the first three weeks were classified by a radiologist (O.K.) according to the scheme presented in table II. This scheme grades the severity of RDS, presence of respiratory complications (pulmonary air leaks) and signs of "early" (age $\leq$ two weeks) or "late" (age $<$ two weeks) cardiac decompensation associated with respiratory distress. The risk odds ratios (RORs) of these items in relation to the later development of BPD were then estimated.

2.4 Statistical methods

All statistical analyses were performed by SPSS [16]. Statistics relating to qualitative variables were analyzed using the chi square test with YATE's correction. Statistics relating to quantitative variables were analyzed using STUDENT's t-test, or if the distribution was not normal, with the median test. The effects of neonatal variables regarding the development of BPD were estimated by means of multiple logistic regression analysis [16]. By this method, estimates of the binary outcome variable (presence vs. absence of BPD) were calculated using either the complete model consisting of all pertinent neonatal variables or various subsets of variables. The sum of squares of deviation from the mean was calculated both for the outcome variable and its estimates. The degree to which the estimates were able to explain the variability of the observed outcome status was expressed as a coefficient of determination, calculated as the ratio of the corresponding sums of squares [17]. Similarly, the effects of early radiologic items on the future development of BPD were assessed. The risk odds ratios (RORs) which indicate the risk of subsequent BPD associated with individual explanators (examined in the presence of other variables) were calculated by multiple logistic regression analysis, using the equation exp(coeff) [16].

3 Results

3.1 RDS and BPD in the preterm cohort

RDS was diagnosed in 46% of preterms born at or before 32 weeks of gestation but only in 4.4% of those born after that date.

Table II. Early radiologic characteristics examined in relation to subsequent development of BPD.

Initial severity of RDS:	Severe = massive alveolar atelectasis (cardiac silhouette not distinguishable from lung parenchyma) Moderate = typical reticulogranular pattern Mild = minimal reticulogranular changes
Respiratory complications:	Pulmonary air leaks Pneumonias or atelectases during respirator treatment
"Early" cardiologic signs:	Cardiac enlargement or pulmonary vascular congestion during the first 2 weeks of life
"Late" cardiologic signs:	Cardiac enlargement or pulmonary vascular congestion after the age of 2 weeks

During the study period 16 cases of BPD were diagnosed. All BPD cases required respirator treatment after birth. Initially, the majority of cases (15 of 16 children with BPD) had typical RDS. Thus, the present study, like the original description of NORTHWAY et al. [12], concentrates on BPD which develops as an extension of RDS. Another type of chronic lung disease which develops after no or minimal respiratory symptoms in preterm infants [18, 19] was possibly present in only one child (gestational age 27 weeks, birth weight 1210 g), who needed three days of respirator care because of very mild respiratory problems and had minimal radiologic signs of RDS. At the age of 28 days, all BPD cases exhibited typical diagnostic features: respiratory difficulties, increased oxygen requirement and pulmonary infiltrates [6].

The usual radiologic picture of BPD was considerably different from extensive cystic abnormalities described in the past [12]. Only three of 15 BPD cases conformed to the very nonhomogeneous and hyperinflated appearance of NORTHWAY's classical Stage four [12]. In the majority of cases (13 out of 16), the ultimate form of pulmonary affection consisted of homogeneous interstitial densities (sometimes combined with irregular, bubbly changes) which obscured vascular markings and extended to the periphery of the lungs.

In all, the incidence of BPD was one case per 1000 live births, or 25 cases per 1000 liveborn preterms. The incidence was highest (135 per 1000) among preterms born at or before 32 weeks of gestation. The majority of BPD cases (127 cases per 1000) developed after typical RDS, while eight cases per 1000 were detected after exceptionally mild respiratory distress and very short respirator treatment.

The overall mortality of preterms born at or before 32 weeks was 22.8%. Both mortality and the occurrence of BPD declined sharply in relation to advancing gestational age (figure 1). Only three cases of postneonatal death occurred among these children, two of which were solely due to BPD and associated cardiac decompensation (cor pulmonale).

3.2 Intrauterine growth status and BPD

Even when compared with preterms of equally low mean gestational age (table III), BPD preterms were significantly lighter. This finding was confirmed by analyzing their birth weights standardized for each gestational week group using

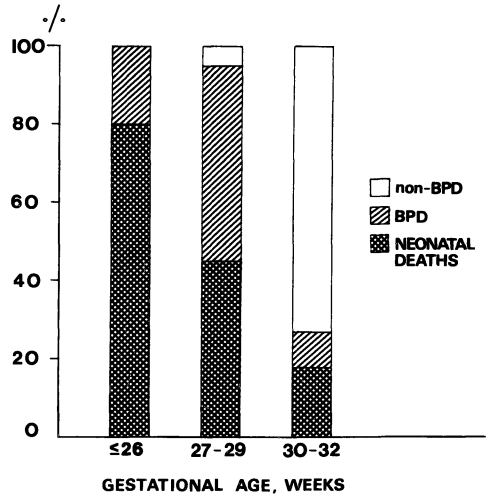

Figure 1. Proportions of non-BPD and BPD survivors and deaths among three gestational age groups (≤ 26, 27–29, 30–32 weeks).

corresponding means and standard deviations (SDs) of non-BPD children. Thus, for each gestational age group, the standardized mean birth weight of non-BPD children was 0 (SD 1), whereas the standardized mean birth weight of BPD children was significantly lower at −0.67 (SD 1.1) ($p < 0.05$).

3.3 Neonatal morbidity and BPD

After birth the morbidity of BPD children was markedly higher than that of non-BPD groups (examined either separately or together) (table I). In particular, BPD children had more perinatal asphyxia, more neurologic symptoms, prolonged need for high (100%) oxygen and more pneumonias than their non-BPD counterparts. BPD children also differed from non-BPD children in respect of requirements and duration of special neonatal care (table IV). In the non-BPD groups, the requirements and duration of neonatal care were similar despite of different gestational maturity.

3.4 Neonatal variables as predictors of BPD

In spite of several significant differences, few neonatal variables were in fact useful clinical predictors of BPD. The neonatal items presented in table V explained 88% of the observed variance of outcome status (that is, presence or absence of BPD at the age of 28 days). The "best" predictors for subsequent development of BPD were prolonged

Table III. Characteristics of BPD and non-BPD children.

Item	BPD	non-BPD			
	n = 16	≤ 30 weeks n = 26	31–32 weeks n = 49	p_1	p_2
Male sex	56%	58%	61%	ns	ns
Mean gestational age (SD), weeks	28.3 (1.6)	29.0 (1.3)	32.0 (0.6)	ns	< 0.001
Mean birth weight (SD), g	1202 (313)	1445 (281)	1822 (388)	< 0.01	< 0.001
Mean birth length (SD), cm	37.0 (4.7)	40.6 (2.7)	43.1 (4.1)	< 0.01	< 0.001
Mean head circumference (SD), cm	26.1 (1.9)	27.6 (1.3)	30.6 (1.9)	< 0.01	< 0.001

p_1 = significance of difference between BPD vs. non-BPD ≤ 30 weeks
p_2 = significance of difference between non-BPD ≤ 30 weeks vs. non-BPD 31–32 weeks

Table IV. Details of neo- and postneonatal hospital care of BPD and non-BPD children.

	BPD	non-BPD			
	n = 16	≤ 30 weeks n = 26	31–32 weeks n = 49	p_1	p_2
Neonatal Care					
Percentage of children requiring respirator treatment	100%	61%	38%	< 0.01	ns
Median duration (range) of respirator treatment, days	12 (3–155)	4 (1–18)	5 (1–18)	< 0.001	ns
Median duration (range) of > 40% oxygen requirement, days	6 (1–39)	2 (1–7)	3 (1–10)	< 0.01	ns
Proportion of children requiring 100% oxygen for > 24 h after birth	39%	3%	2%	< 0.05	ns
Median duration (range) of neonatal hospitalization	102 (64–554)	56 (19–84)	37 (7–142)	< 0.001	< 0.01
Readmissions					
None	31%	69%	53%	< 0.01	ns
1–5	44%	31%	41%		
> 5	25%	0%	6%		
Overall median duration (range) of readmission(s), days	25 (11–657)	4 (3–138)	7 (2–188)	< 0.05	ns

p_1 = significance of difference between BPD-group vs. non-BPD ≤ 30 weeks
p_2 = significance of difference between non-BPD ≤ 30 weeks and non-BPD 31–32 weeks

(> 24 h) need for 100% oxygen after birth, presence of pneumonias and low (< 7) five-minute Apgar score. These variables explained 78% of the observed variance of outcome status.

3.5 Early radiologic signs as predictors of BPD

Early radiologic predictors (table VI) of BPD explained 57% of the variance of outcome status.

Table V. Clinical items as predictors of BPD.

Item	Regr. coefficient	Coeff/SE	ROR	p
Constant	−1.71			
Low 5 minute Apgar score	1.60	1.76	5.0	ns
Pneumonias during respirator treatment	2.78	3.11	16.1	< 0.005
Need for 100% oxygen for > 24 h after birth	3.44	3.29	31.2	< 0.001
Pulmonary air leaks	1.30	1.04	3.7	ns
Convulsions or apneic episodes	1.00	1.95	2.7	ns
	Coefficient of determination[1]			
All items		0.88		
Low 5 minute Apgar score, need for 100% oxygen for > 24 h after birth, pneumonias		0.78		

[1] Ratio of explained variance to the total observed variance of outcome status

Table VI. Early radiologic items as predictors of BPD.

Item	Regr. coefficient	Coeff/Se	ROR	p
Constant	−1.26			
Presence of massive alveolar atelectasis	2.58	2.52	13.2	< 0.01
Presence of "early" cardiac enlargement	1.48	1.62	4.3	ns
Presence of pulmonary air leaks	−1.32	−1.0	0.26	ns
Presence of "late" cardiac enlargement	1.96	1.36	7.2	ns
"Late" pulmonary vascular engorgement	−1.50	−0.75	0.22	ns
	Coefficient of determination[1]			
All items		0.57		
Massive alveolar atelectasis and "early" cardiac enlargement		0.54		

[1] Ratio of explained variance to the total observed variance of outcome status

The "best" predictors together (presence of severe alveolar atelectasis at birth and cardiac enlargement during the first two weeks of life) explained 54% of the variance of outcome status.

3.6 Postneonatal morbidity associated with BPD

Preterms with BPD had markedly higher morbidity, also during the postneonatal period (up to two years), than the non-BPD children (table IV). This includes not only chronic prematurity-associated conditions but also hospital readmissions because of intermittent short-term care, particularly for respiratory infections. All subgroups of respiratory tract infections were more common among BPD children than their non-BPD counterparts (figure 2).

Among the BPD group, the proportion of children with one or more readmissions to hospital was significantly greater than among non-BPD groups (table IV). The median duration of postneonatal hospital care was significantly longer in the BPD group than in either of the non-BPD groups. On the other hand, the overall duration of readmissions among both non-BPD groups was equally short in spite of their different gestational maturity. In all, the BPD group, which consisted only

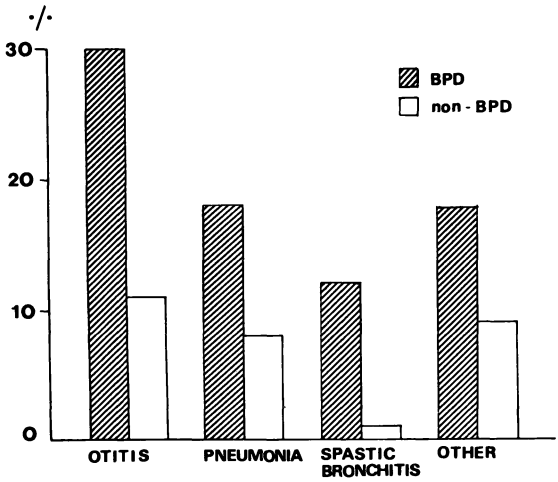

Figure 2. Percentage of non-BPD and BPD preterms suffering from various respiratory infections during the first two years of life.

of 18% of all neonatal survivors born at ≤ 32 weeks consumed 53% of all hospital days used in the postneonatal care of these children during the first two years of life.

4 Discussion

An appropriate definition of the population "at risk" for BPD is clearly of prime importance for comparative purposes and the planning of interventions. Gestational immaturity is the main prerequisite for the development of BPD [3]. Similarly to previous reports [4, 6], we decided not only to relate the occurrence of BPD to a complete preterm birth cohort but also to explore more precise defintions for the population at risk. In a previous study [6], this population was defined by low birth weight (< 1500 g), the incidence of BPD among such preterms being 140 cases per 1000. Instead of birth weight we used gestational age (≤ 32 weeks) and detected a remarkably similar incidence of 135 BPD cases per 1000 preterms born at or before 32 weeks. While all BPD cases were born at or before 32 weeks, the majority (88%; 14 of 16 BPD children) would have been detected even if birth weight < 1500 g had been used as the cutoff point. Thus, either of the above definitions (birth weight < 1500 g or gestational age ≤ 32 weeks) seems appropriate for identifying the preterm population at risk for BPD.

Our cases with BPD were mainly derived from preterms who suffered from typical RDS after birth. Only one of 16 cases had a history of minimum respiratory distress and very short respiratory treatment before clinical and radiologic signs of BPD slowly appeared. The incidence of such "chronic lung disease of prematurity" [18, 19] was much lower than that of BPD developing after typical RDS in our preterm birth cohort (8/1000 vs. 127/1000, respectively). More data on both types are required to estimate more reliably the overall occurrence of chronic lung disorders of prematurity and to clarify possible differences in their pathophysiologic mechanisms [3].

According to our experience, reliable identification of individual BPD candidates early in the course of disease seems rather difficult. While simple clinical indicators of grave respiratory distress (e. g. prolonged need for 100% oxygen immediately after birth) are associated with a high relative risk for BPD, the predictive value of other aspects of neonatal morbidity regarding the future development of BPD is weak. Further radiologic classification of RDS as severe, moderate or mild, as well as the grading and timing of accompanying cardiologic signs did not enhance their predictivity. However, the present data suggest that restricted intrauterine growth (IUGR) deserves further investigation as a possible risk factor of BPD. The unfavourable effects of IUGR on neonatal well-being [20, 21] and on the developmental prospects [22, 24] of preterm infants have also been recently established.

The follow-up of BPD children should receive adequate attention. Paradoxically, the initial course of BPD survivors during the neonatal period may even appear favorable, being characterized by a gradually declining need for supplementary oxygen [4, 6, 7]. In this study the majority (75%) of BPD cases were weaned off oxygen before term, and none were sent home on oxygen [11]. Still, even after discharge from the neonatal intensive care unit the BPD group continued to use more hospital care than their non-BPD counterparts, in particular for various respiratory infections. Respiratory problems are, however, only one facet of BPD-associated postneonatal morbidity. In our study, all preterms with retrolental fibroplasia belonged to the BPD group. More than one third of BPD survivors had some form of neurologic sequelae. This is in accordance with previous reports [4, 25], which have also shown a

predominance of milder neurologic problems in BPD children at preschool age [26]. In order to detect such problems, appropriate tests before school entrance are necessary [24], and should be arranged for every BPD patients as for other severely ill newborns.

Abstract

The occurrence, predictive factors and associated morbidity of bronchopulmonary dysplasia (BPD) was examined in a preterm birth cohort of 712 children, born before 37 weeks of gestation to residents of a geographically defined area between 1978–82. All cases of BPD (N = 16) were born at or before 32 weeks of gestation. The incidence of BPD, based on status at the age of 28 days, was 1 per 1000 live births, but 135 per 1000 live preterms born at or before 32 weeks. Most cases of BPD developed following respiratory distress syndrome (RDS), only one case developing after minimal respiratory symptoms was observed. BPD infants had higher neonatal morbidity, even when compared with preterms of equal gestational maturity, but only a few variables had predictive value with respect to the future development of BPD. Radiologic grading of RDS and associated early cardiologic signs did not increase their predictivity regarding the subsequent development of BPD. Two (12.5%) of the 16 BPD infants died postneonatally. The unfavorable effects of BPD on the health status of preterm infants extended far beyond the neonatal period. The BPD group, which consisted only of 18% of neonatal survivors born at $\leq$ 32 weeks, consumed 53% of all hospital days used by these preterms during the first two years of life. In particular, BPD survivors had markedly more respiratory infections (63%), more neurologic sequelae (37%) and more cases of retrolental fibroplasia (12%) than their non-BPD counterparts.

Keywords: Bronchopulmonary dysplasia, preterm infants.

Zusammenfassung

Inzidenz, prädiktive Faktoren und Morbidität von bronchopulmonalen Dysplasien bei Frühgeborenen

Beschrieben wird die Inzidenz von bronchopulmonalen Dysplasien (BPD) in einem Kollektiv von Frühgeborenen, das in der Provinz Kuopio, Finnland, in dem Zeitraum 1978–1982 entbunden wurde. In dieser Provinz ist die Frühgeburtenrate gering, es gibt eine vom Staat subventionierte Schwangerenvorsorge und regionale geburtshilfliche und neonatale Versorgungseinheiten. Wir untersuchten den prädiktiven Wert verschiedener perinataler Parameter und früher radiologischer Zeichen im Hinblick auf die Entwicklung einer BPD. Darüberhinaus wurde der Einfluß einer BPD auf die postnatale Morbidität überprüft.

Während des Untersuchungszeitraums wurde in einem Kollektiv von 712 Frühgeborenen in 16 Fällen eine BPD diagnostiziert. Alle diese Kinder wurden mit oder unter 32 Schwangerschaftswochen geboren. Die Inzidenz betrug damit 135 auf 1000 lebende Frühgeborene. Post partum hatte die Mehrzahl dieser Kinder (15 von 16) ein typisches RDS. Eine andere Form der chronischen Lungenerkrankung im Zusammenhang mit Prämaturität entwickelte sich möglicherweise bei einem Frühgeborenen ohne ernsthafte respiratorische Probleme. Mit einem Gestationsalter von 27 Wochen und einem Geburtsgewicht von 1210 g genötigte es eine dreitägige respiratorische Überwachung wegen geringfügiger Symptome bei minimalen radiologischen Zeichen eines RDS.

Das radiologische Bild einer BPD unterschied sich beträchlich von denen, die ausgedehnte cystische Veränderungen beschreiben. Lediglich in drei Fällen konnten wir solche Befunde, wie sie in der Vergangenheit erhoben wurden, sehen. In der Mehrzahl der Fälle (13 von 16) fanden wir letztlich Formen mit ziemlich homogenen interstitiellen Verdichtungen (manchmal im Kombination mit unregelmäßigen bläschenförmigen Veränderungen), die vaskuläre Abschnitte nicht erkennen ließen und sich bis zur Lungenperipherie hin erstreckten.

Post partum war die Morbidität der BPD-Kinder höher als in den Gruppen ohne BPD. Eine hohe prädiktive Aussagekraft für eine sich einstellende BPD hatten eine perinatale Asphyxie, verlängerter Bedarf an 100%igem O_2 post partum und Auftreten von Pneumonien. Diese Variablen zusammen erfassen 78% der Varianz beim endgültigen Krankheitsbild. Das radiologische Grading sowie damit assoziierte kardiologische Parameter konnten nicht die Aussagekraft der o. g. Faktoren im Hinblick auf die weitere Entwicklung der BPD erhöhen. In der Postneonatalperiode, bis zum Alter von 2 Jahren, waren rezidivierende Infektionen der Atemwege (63%), neurologische Auffälligkeiten (37%) und retrolentale Fibroplasien (12%) in der BPD-Gruppe häufiger als in der Kontrollgruppe bei gleichem Gestationsalter. Die mit einer BPD assoziierte postneonatale Mortalität betrug 12%.

Die vorliegenden Daten zeigen, daß entweder ein Gestationsalter von $\leq$ 32 Wochen oder ein Geburtsgewicht $<$ 1500 g sich gut dafür eignen, um in einer Frühgeborenengruppe Risikokinder für eine BPD zu selektionieren. Mit dem Gestationsalter wären in unserer Studie alle Kinder mit BPD erfaßt worden, während bei Verwendung des Geburtsgewichts $<$ 1500 g als Diskrimi-

nante immerhin auch noch 14 von 16 Kindern (88%) als Risikokinder eingestuft wären. Die sich nach einer typischen RDS-Symptomatik einstellende BPD war wesentlich häufiger (Inzidenz 127 auf 1000) als die "chronische Lungenerkrankung bei Prämaturität", wie sie nach geringfügigen respiratorischen Problemen auftritt (Inzidenz 8 auf 1000). Hinsichtlich beider Typen von Lungenerkrankungen werden jedoch dringend mehr Daten benötigt, um das Gesamtauftreten chronischer pulmonaler Störungen bei Frühgeborenen zu erfassen und mögliche Unterschiede bezüglich deren pathophysiologischer Mechanismen aufzuklären. Auch den Nachuntersuchungen von Kindern mit BPD sollte mehr Aufmerksamkeit geschenkt werden, um die längerfristige und weitergefaßte Morbidität in Assoziation mit diesem Krankheitsbild besser erfassen zu können.

Schlüsselwörter: Bronchopulmonale Dysplasie, Frühgeborene.

Résumé

Occurence, facteurs prédictifs et morbidité liés à la dysplasie broncho-pulmonaire au sein d'une cohorte de naissances prématurées

Nous décrivons l'occurrence de la dysplasie bronchopulmonaire (D. B. P.) dans une cohortede prématurés nés dans la Province de Kuopio en Finlande au cours des années 1978–1982. La zone de l'étude est caractérisée par un taux faible de prématurité, par des soins prénataux pris en charge par le gouvernement et par une régionalisation des services d'Obstétrique et de Néonatologie.

La valeur prédictive des facteurs périnataux et les critères radiologiques précoces en relation avec le développement ultérieur d'une D. B. P. ont été étudiés. Au total, nous avons examiné l'impact de la D. B. P. sur la morbidité post-néonatale. Au cours de la période de l'étude, on a diagnostiqué 16 cas de D. B. P. au sein d'une cohorte de naussances prématurées concernant 712 enfants. Tous les enfants atteints de D. B. P. sont nés à ou avant 32 semaines de gestation. L'incidence de la D. B. P. est de 135 pour 1000 naissances vivantes chez les prématurés nés à ou avant 32 semaines de gestation.

Après la naissance, la majorité des cas (15 des 16 enfants avec D. B. P.) présente un symdrome de détresse respiratoire (S. D. R.) typique.

Un autre type d'affection pulmonaire chronique du prématuré qui survient sans ou avec un minimum de symptômes respiratoires chez les prématurés s'est peut-être mainifesté chez un enfant (de 27 semaines d'âge gestationel, et le poids de naissance de 1210 g) qui a nécessité trois jours d'assistance respiratoire en raison de problèmes respiratoires très légers et qui a présenté seulement de minimes signes radiologiques de S. D. R.

Les aspects radiologiques habituels de D. B. P. sont très différents des anomalies kystiques disséminées décrites dans le passé, et il n'y a que trois des 16 cas de D. B. P. qui étaient conformes aux descriptions antérieures. Dans la majorité des cas (13 sur 16), la forme évoluée comporte plutôt des densifications interstitielles homogènes (parfois associées à des aspects bulleux irréguliers) qui diminuent la trame vasculaire et s'étendent jusqu'aux zones pulmonaires périphériques. Après la naissance, la morbidité des enfants avec D. B. P. est plus élevée que dans le groupe sans D. B. P. (étudiés séparément ou globalement). Les meilleurs marqueurs prédictifs du développement ultérieur de D. B. P. sont l'asphyxie périnatale, le besoin prolongée d'oxygénothérapie à 100% après la naissance et la présence de pneumonie. Ensemble, ces variables expliquent 78% de la variance de l'évolution. Le grading radiologique de la sévérité de la D. B. P. et les signes cardiaques associés n'augmentent pas la prédictivité pour le développement futur de D. B. P.

En période post-néonatale, jusqu'à l'âge de deux ans les infections à répétition de l'arbre respiratoire (63%), les séquelles neurologiques (37%) et la fibrodysplasie rétrolentale (12%) sont plus fréquentes chez les prématurés avec D. B. P. que chez les enfants de maturité gestationnelle similaire sans D. B. P. La mortalité post-néonatale des D. B. P. est de 12%.

Ces données montrent que soit un âge gestationnel $\leqslant 32$ semaines soit un poids de naissance < 1500 g peuvent être utilisés pour définir des populations de prématurés à risque de D. B. P. Tandis que tous nos cas de D. B. P. sont nés à ou avant 32 semaines de gestation, la majorité (88%; 14 des 16 enfants avec D. B. P.), aurait été detectée si un poids de naissance < 1500 g avait été utilisé comme limite.

Les D. B. P. se développant après un S. D. R. typique sont plus havituelles (incidence de 127 pour 1000) que la «maladie pulmonaire chronique du prématuré» qui apparait lentement après peu ou pas de symptomes respiratoires (incidence de 8 pour 10). De plus amples données sur les deux types sont encore nécessaires et de façon urgente pour confirmerl'occurence globale des affections pulmonaires chroniques chez les prématurés et pour clarifiér les différences possibles de leurs mécanismes physio-pathologiques. Il faudrait preter plus d'attention au suivi des prématurés avec D. B. P. pour combattre la morbidité à long terme et à large spectre qui accompagne cette pathologie.

Mots-clés: Dysplasie broncho-pulmonaire, prématurés.

References

[1] GITLIN JD, RF SELL, RB PARAD, JD HORBAR, HA FELDMAN, JF LUCEY, HW TAEUSCH: Randomized controlled trial of exogenous surfactant for the treatment of hyaline membrane disease. Pediatrics 79 (1987) 31

[2] MERRITT TA, M HALLMAN, BT BLOOM, C BERRY, K BERNISCHKE, D SAHN, T KEY, D EDWARDS, A-L JÄRVENPÄÄ, M POHJAVUORI, et al: Prophylactic treatment of very premature infants with human surfactant. N Engl J Med 315 (1986) 785

[3] EDWARDS DK: Bronchopulmonary dysplasia today. Adv Perinat Med 3 (1983) 117

[4] YU VYH, AA ORGILL, SB LIM, B BAJUK, J ASTBURY: Growth and development of very low birthweight infants recovering from bronchopulmonary dysplasia. Arch Dis Child 58 (1983) 791

[5] VON TOSCH U, C BECKER-GAAB, C DACHS: Die Häufigkeit der bronchopulmonalen Dysplasie im Verlauf des Atemnotssyndroms bei Frühgeborenen. Fortschr Röntgenstr 141 (1984) 167

[6] TOCE SS, PM FARRELL, LA LEAVITT, DP SAMUELS, DK EDWARDS: Clinical and roentgenographic scoring systems for assessing bronchopulmonary dysplasia. Am J Dis Child 138 (1984) 581

[7] TRUOG WE, JC JACKSON, RJ BADURA, GK SORENSEN, JH MURPHY, DE WOODRUM: Bronchopulmonary dysplasia and pulmonary insufficiency of prematurity. Am J Dis Child 139 (1985) 351

[8] AVERY MA, WH TOOLEY, JB KELLER, et al: Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. Pediatrics 79 (1987) 26

[9] HARTMANN JF, F BEAUFILS, C VERVEL: Prognostic factors in severe bronchopulmonary dysplasia. A retrospective study of 65 premature infants with bronchopulmonary dysplasia. Ann Fr Pediatr 44 (1987) 423

[10] Perinatal Status 1975. Perinatal committee report. Finnish Medical Association – Helsinki 1978

[11] HAKULINEN A, K HEINONEN, V JOKELA, K LAUNIALA: Prematurity-associated morbidity during the first two years of life. Acta Paediatr Scand 77 (1988) 340

[12] NORTHWAY WH, RC ROSAN, DY PORTER: Pulmonary disease following respirator therapy of hyaline membrane disease. N Engl J Med 276 (1976) 357

[13] D'AVIGNON M, B BILLE, B HAGBERG, I OLOW: Clinical classification of cerebral palsy in childhood. Läkartidningen 57 (1960) 2533

[14] PATZ A: The new international classification of retinopathy of prematurity. Pediatrics 74 (1984) 160

[15] KLEINBAUM DG, LL KUPPER, H MORGENSTERN: Epidemiological research. Principles and quantitative methods. van Nostrand Reinhold Company, New York 1982

[16] SPSSx: Users guide: 2nd edition. McGraw-Hill Book Company, New York 1986

[17] SPIEGEL MR: Theory and problems of statistics, Schaum Publishing Company, New York 1961

[18] WILSON, M, V MIKITY: A new form of respiratory disease in premature infants. Am J Dis Child 99 (1960) 489

[19] KRAUSS A, D KLEIN, P AULD: Chronic pulmonary insufficiency of prematurity. Pediatrics 55 (1975) 55

[20] STARFIELD B, M MCCORMICK: Mortality and morbidity in infants with intrauterine growth retardation. J Pediatr 101 (1982) 978

[21] HEINONEN K, R MATILAINEN, H KOSKI, K LAUNIALA: Intrauterine growth retardation (IUGR) in preterm infants. J Perinat Med 13 (1985) 171

[22] CALAME A, S DUCRET, L JAUNIN, B PLANCHEREL: High risk appropriate for gestational age (AGA) and small for gestational age (SGA) preterm infants. Helv Paediatr Acta 38 (1983) 39

[23] COMMEY JOO, PM FITZHARDINGE: Handicap in the preterm small-for-gestational age infant. J Pediatr 94 (1979) 779

[24] MATILAINEN R, K HEINONEN, H TIUSANEN-SIREN, V JOKELA, K LAUNIALA: Neurodevelopmental screening of in utero growth-retarded prematurely-born children before school age. Eur J Pediatr 146 (1987) 453

[25] HORWOOD SP, MH BOYLE, GW TORRANCE, JC SINCLAIR: Mortality and morbidity of 500–1499 g birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. Pediatrics 69 (1982) 613

[26] SAUVE RS: Long-term morbidity of infants with bronchopulmonary dysplasia. J Behav Rev Pediatr 4 (1983) 243

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